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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/500,700	02/09/2000	Carlos F. Barbas III	SCRIP1160-4	2975

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EXAMINER

LEFFERS JR, GERALD G

ART UNIT	PAPER NUMBER
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1636

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DATE MAILED: 08/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/500,700

Applicant(s)

BARBAS III ET AL.

Examiner

Gerald G Leffers Jr., PhD

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2003.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5, 16-19, 40 and 42-45 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 2-5, 16-19 and 40 is/are allowed.
- 6) ☒ Claim(s) 42-45 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Receipt is acknowledged of an amendment, filed 6/13/03 as Paper No. 29, in which several claims were amended (claims 2, 16 and 42). Claims 2-5, 16-19, 40 and 42-45 are pending in the instant application.

Response to Amendment

Any rejection of record in the previous office action (Paper No. 27 mailed 3/11/03) not addressed herein is withdrawn. This action is not final due to additional grounds of rejection made herein that were not necessitated by applicants' amendment of the claims in Paper No. 29.

Receipt is acknowledged of terminal disclaimers filed over U.S. Patent Nos. 6,140,466 and 6,242,568. The terminal disclaimers filed on 6/13/03 as part of Paper No. 28, disclaiming the terminal portion of any patent granted on this application that would extend beyond the expiration dates of the patents cited above, have been reviewed and are accepted. The terminal disclaimers have been recorded. This response has obviated the Obviousness Double Patenting rejections made in the previous office action.

The statutory double patenting rejection made in Paper No. 27 against claim 40 has been withdrawn in response to applicants' arguments in Paper No. 29. Applicants correctly note that claim 46 of U.S. Patent No. 6,242,568 recites the limitation "...wherein each of two modules of said variant has at least one amino acid sequence modification." Claim 40 of the instant application differs in that it recites "...wherein at least one of the at least two modules of said variant has at least one amino acid sequence modification." It is noted that a terminal disclaimer has been filed over U.S. Patent No. 6,242,568. If no such disclaimer had been entered, however,

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claim 40 would be rejectable under Obviousness Double Patenting over claims 1 and 46 of the patent. The patent claims are species claims (i.e. "wherein each of two modules") embraced by, and which anticipate, claim 40 of the instant application (i.e. "at least one of the at least two modules"). Because the terminal disclaimer has already been entered into the file, the issue is moot.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **The instant rejection is maintained for reasons of record in Papers No. 10, 17 and 27. The original grounds of rejection in Paper No. 10 are summarized below.**

Claims 42-46 are directed towards a "hybrid" zinc finger protein that binds to a target nucleic acid, the hybrid zinc finger comprising zinc fingers from a first protein linked to zinc fingers from a second protein and whereby the hybrid protein binds a nucleic acid sequence different from that bound by any of the individual modules of the first and second proteins. A reasonable interpretation of the claim language includes embodiments wherein at least two zinc fingers from a zinc finger protein of one type (e.g. Zif268) and two zinc fingers from a protein of

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another type (e.g. TFIIIA). The fingers can be “variants” of the parental donor fingers. The “variants” can be mutagenized forms of the parental donor fingers. The hybrid zinc finger protein can modulate expression of the target nucleic acid. The amino acid sequence of each finger can comprise two cysteines and two histidines with both cysteines are amino proximal to both histidines. The rejected claims encompass an enormous genus of possible combinations of zinc finger modules obtained from literally any zinc finger protein that must retain the ability to bind a sequence different from a sequence bound by individual modules of the first protein and the second protein.

The specification exemplifies the zinc finger variants of the invention in terms of two known zinc finger proteins, Zif268 and TFIIIA. No other zinc finger proteins are described in detail in the specification. No description or relevant working example is provided wherein the zinc finger protein variant is a “hybrid” comprising fingers obtained from different types of proteins. In other words, no single embodiment of the claimed invention has been described in the specification. No significant description is provided of what such hybrid proteins would look like except to specify that the proteins would have zinc fingers obtained from different sources. The specification merely asserts that such recombinant hybrid proteins are feasible. No description is provided of which zinc finger modules from which sources would be desirable for recombination to produce a “hybrid” zinc finger protein. No description is provided of specific changes to generate “variants” that necessarily bind a given sequence that is not bound by a zinc finger nucleotide binding protein that lacks amino acid sequence modification. A single preferred linking domain, the 5 amino acid sequence TGEKP, is suggested for linking zinc finger modules in construction of the variant proteins of the invention. No other potential linking

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domain is described. No description is provided of other domains from any other zinc finger protein that would be retained in such any hybrid protein of the invention. Therefore, there is no basis provided by the specification for one of skill in the art to envisage a representative number of embodiments of the claimed invention that meet the functional limitations recited in the amended claims.

The prior art does not appear to rectify the deficiencies of the instant specification regarding the claimed invention. The claimed invention does not appear to have been described in the prior art. While zinc finger proteins are and were known in the art, the combination of zinc finger modules to construct recombinant proteins does not appear to have been routinely practiced at the time of applicants invention. Nor does there appear to be a sufficient number of examples where "variant" zinc finger nucleotide proteins that retain an ability to specifically bind a given sequence that is not bound by a non-mutant zinc finger protein so that one of skill in the art has a structural/functional basis to envision those mutated variants that will meet the functional limitations of the claims.

Given the factors outlined above, one of skill in the art would not have been able to envisage a representative number of embodiments of such hybrid proteins or "variants" to describe the claimed genus that meet the functional limitations of the claims. Therefore, one of skill in the art would reasonably have concluded that applicants were not in possession of the claimed invention.

Response to Arguments/Written Description Claims 42-45

Applicant's arguments filed in Paper No. 29 have been fully considered but they are not persuasive. The response essentially argues 1) the specification defines the term "variant" in

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terms of the claimed hybrid zinc finger proteins at page 10, 2) one of skill in the art would have been able to take the teaching of a hybrid variant and combine it with the teachings of the application (e.g. page 43, lines 21-31), 3) one of skill in the art would be able to take the particular teachings of the invention where the variant is a modified natural amino acid sequence with a new binding specificity and apply them to a situation where the variant is a hybrid.

The definition of the term variant provided by the specification does not provide a basis for one of skill in the art to envision a sufficient number of specific embodiments (e.g. primary amino acid sequence) that would meet the functional limitations of the claims. The remaining arguments are directed to the ability of one of skill in the art to make the claimed zinc finger hybrids. These arguments are better directed to an enablement rejection rather than the written description rejection maintained here.

Claims 42-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This rejection is maintained for reasons of record in Paper No. 27, mailed 3/11/03 and repeated below.**

Each of the claims comprises a new limitation wherein the claimed hybrid variant binds to a polynucleotide sequence different from a sequence bound by individual modules of the first protein and second protein from which the hybrid is constructed. There does not appear to be support anywhere in the specification as originally filed for this limitation. Therefore, this limitation is impermissible NEW MATTER.

Response to Arguments

Applicant's arguments filed in Paper No. 29 have been fully considered but they are not persuasive. The response points to specific passages from the originally filed disclosure for support for the concept that the modules of the hybrid zinc finger protein do not bind to sequences recognized by either of the proteins from which the hybrid is derived. The passages cited in the response do not support the assertion that there is support for the claimed subject matter in the originally filed specification. The limitation cited in making the rejection is a very specific functional limitation that the hybrid zinc finger protein binds a sequence different from a sequence bound by individual modules of the first and second protein. The examiner can find no support in the originally filed specification for the limitation that the hybrid protein does not bind a sequence bound by individual modules obtained from the first and second proteins used to generate the hybrid protein.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 42-45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. **The following are new rejections.**

Claim 42 is vague and indefinite in that there is no clear and positive prior antecedent basis for the phrase "each zinc finger protein" in line 6 of the claim. It appears that the term "module" should follow the cited phrase.

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Claim 42 is further vague and indefinite in that the metes and bounds of the phrase "...a sequence bound by individual modules of the first protein and second protein..." are unclear. It is unclear if the bound sequence is one that binds modules from both the first and second protein, or if the phrase is meant to specify more than one sequence, each bound by either the first or second proteins.

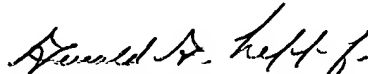
Conclusion

Claims 2-5, 16-19 and 40 are allowable. Claims 42-45 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr., PhD whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.


Gerald G Leffers Jr., PhD
Examiner
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